REMARKS

Claim Status

Claims 2-16, 19, 20, and 22 are pending after entry of this paper. Claims 2-8 have been rejected. Claims 9-16, 19-20 and 22 have been withdrawn and claims 1, 17-18 and 21 have been previously cancelled without prejudice. Applicants reserve the right to pursue withdrawn and cancelled claims in a continuing application. Claims 2-8 have been amended.

Claim 2 has been amended to add the term "HLA-DR." Support may be found throughout the instant specification, for instance, applicants wish to direct the Examiner's attention to Example 20 and Table 2.

No new matter has been introduced by these amendments. Reconsideration and withdrawal of the pending rejections in view of the above claim amendments and below remarks are respectfully requested.

Response to Rejections under 35 U.S.C. §102(b)

Claims 2-8 have been rejected under 35 U.S.C. §102(b) as being anticipated by Zhao, et al. (*PNAS,* 100: 2426-2431, 2003). Specifically, the Examiner contends that Zhao allegedly discloses the isolation of pluripotent stem cells (PSC) from human peripheral blood monocytes that resemble fibroblasts and express the monocytic and hematopoietic cellular differentiation stem cell markers, such as CD14, CD34 and CD45. While Zhao does disclose that PSCs express type I collagen, according to the Examiner, it would be inherent (Office Action – page 3). Therefore, the Examiner concludes that Zhao allegedly anticipates the claimed invention (Office Action – page 3). Applicants respectfully disagree.

In the previous response filed on August 29, 2008, applicants duly filed a set of claims in view of Examiner Stucker's advice during the interview held between the applicants, Examiner Dutt and Supervisory Examiner Stucker. The claims incorporated the features of the method of preparing MOMC. Further, in the Declaration by Dr. Kuwana filed along with the response on August 29, 2008, Dr. Kuwana, the inventor of the instant application, stated and declared that he attempted to induct T cells using IL-2 by the method described in Zhao and that the results demonstrated that CD3 was not expressed and the induction to T-cells failed, to demonstrate the difference in functional characteristics between PSC and MOMC.

The Examiner, nonetheless, concludes in the instant Office Action that applicant's arguments and the inventor's declaration are unpersuasive. Specifically, the Examiner states in reference to the Declaration that

> [a]pplicant demonstrates data showing that MOMC cultured under Zhao conditions do not differentiate to neurons, hepatocytes, or epithelial cells. However, in order to reproduce Zhao result and present a comparison with the instant MOMC, Applicants require to conduct a complete study following the Zhao and instant protocol. As explained above, Zhao's PSC are structurally the same as MOMC, therefore, the cells of the prior art would be functionally the same under identical culture conditions, absent evidence to contrary. Applicant's data do not support such information because Applicant's comparison is incomplete, therefore, inconclusive.

(Office Action, page 7, line 16 – page 8, line 2). The Examiner also states in reference to the marker for collagen I that

> [b]ecause the expression of type I collagen is indicated as :"N/D" and not "-" (N/D is not defined in the article) for PSC, Examiner interprets N/D as not determined; that is, not tested. That the references (Zhao and Seta) are silent on the positive expression of collagen type I, does not prove otherwise, absent evidence to the contrary.

(Office Action, page 5, line 17 – page 6, line 2). Finally, the Examiner concludes while pointing to the disclosure of Seta et al., that PSC and MOMC are identical in that "PSC and MOMC are structurally the same because both cell types express CD14, CD34 and CD45 (Table 1)." (Office Action, page 5). In other words, even though MOMC and PSC are inherently different and their functional characteristics also differ, the Examiner regards PSC and MOMC to be structurally the same merely because both cell types express CD14, CD34 and CD45. Applicants respectfully disagree with Examiner's reasoning and conclusion.

As an initial matter, in order to expedite prosecution and without disclaimer of or prejudice to the subject matter recited therein, applicants have amended claim 2 to add an additional identifier "HLA-DR" which is expressed by the MOMC cells. Support may be found throughout the instant specification, for instance, in Example 20 and Table 2. Applicants respectfully assert that the presently amended claims readily distinguish the claimed multipotent cells (MOMC) from the pluripotent cells (PSC) of Zhao.

Applicants respectfully direct the Examiner's attention to Table 1 of Zhao, which teaches the characteristic markers of f-Mϕ (PSC cell) and s-Mϕ cells. Specifically, Zhao teaches 9 types of surface antigen markers, 7 types of cytokine production markers, 3 types of adipocyte markers and 3 types of functional indicators specific for the above noted cells. Therefore, applicants respectfully assert that in order to ascertain the differences between MOMC and PSC cells, a skilled artisan would not only look at the expression of CD14, CD34 and CD45, but also would look at such identifiers as HLA-DR, HLA-DQ, IL-10 and TNF-α as negative markers for the characterization of f-Mϕ. In fact, Zhao teaches that "the f-Mϕ [PSC cells] diverged from s-Mϕ in that they exhibited reduced levels of IL-10, TNF-a, TNF-RII, HLA-DR, and HLA-DQ (Table 1)," (Zhao et al., page 2427, right column, last paragraph), and "[t]o substantiate their

progenitor nature, we incubated four individual preparations . . . . This treatment transformed the f-Mϕ into s-Mϕ, characterized by their morphology, lipid staining (Figs. 1f and 3), increased HLA-DR, HLA-DQ, IL-10, and TNF-α immunostaining (Fig. 3), and cytotoxic ability." (Zhao et al., page 2428, left column, line 24 – right column, line 3). On the other hand, Example 20 of the instant specification demonstrates that the expression of HLA-DR in MOMC is very high, *i.e.*, strong staining indicated by "+ +" (Table 2). Therefore, since Zhao shows that the HLA-DR marker is negative for f-Mϕ, whereas the same marker is positive for MOMC, a skilled artisan would conclude that PSC cells (f-Mϕ) and MOMC cells are different as presently claimed and are not anticipated by the teachings of Zhao.

Furthermore, Zhao teaches that f-Mϕ (PSC) hardly proliferates unless it is treated with M-CSF (Zhao et al., page 2428, left column, lines 3-12). On the other hand, addition of M-CSF is not required for proliferation of MOMC (Kuwana et al., *Stem Cells* (2006), 2733-2743, page 2734, left column, line 25; respectfully attached for Examiner's consideration). Thus, one skilled in the art could not and would not assume based on the differentiation potential of MOMC and PSC with respect to M-CSF that they are either similar or the same. To argue otherwise, is to ignore the critical elements in functional characterization of MOMC and PSC cells.

Moreover, the Examiner alleges that

> [a]pplicant demonstrates data showing that MOMC cultured under Zhao conditions do not differentiate to neurons, hepatocytes, or epithelial cells. However, in order to reproduce Zhao result and present a comparison with the instant MOMC, Applicants require to conduct a complete study following the Zhao and instant protocol. As explained above, Zhao's PSC are structurally the same as MOMC, therefore, the cells of the prior art would be functionally the same under identical culture conditions, absent

> evidence to contrary. Applicant's data do not support such information because Applicant's comparison is incomplete,

Based on the Examiner's statements, it seems that applicants must reproduce PSC cells in order to conduct a proper comparison. However, applicants assert that the Examiner's conclusion is without merit. Applicants relied on the findings of Zhao as being true, unless the Examiner can provide reasons otherwise, and compared them to the findings presented in the declaration of Dr. Kuwana and the instant application with respect to MOMC. In other words, if applicants attempted to differentiate MOMC cells based on Zhao's methods and arrived at different results, this demonstrates that the underlying cells, *i.e.*, PSC vs. MOMC, are different. The instant inventors attempted to induce differentiation of MOMC into (1) T-cells using IL-2 factor, (2) neuronal cells using nerve growth factor, (3) epithelial cells using epidermal growth factor, and (4) hepatocytes using hepatocyte growth factor as Zhao employed with PSCs. However, the results indicate that MOMCs do not differentiate into T-cells, neuronal cells, epithelial cells or hepatocytes using the methods described in Zhao. Therefore, one skilled in the art could and would deduce that MOMCs are distinct from PSCs (See the previously submitted declaration by Dr. Kuwana).

In light of the amendments to claims, the experimental results presented in the inventor's declaration, and the above arguments, applicants respectfully assert that one skilled in the art would not and could not consider the claimed MOMCs to be the same as the PSCs of Zhao. Hence, the claimed MOMCs are not anticipated by the PSCs of Zhao expressly or inherently because Zhao does not disclose each and every element of the claims as presented

herewith (See MPEP 2131[1]). Reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b) of claims 2-8 as being anticipated by Zhao, et al. are respectfully requested.

Dependent Claims

The applicants have not independently addressed all of the rejections of the dependent claims. The applicants submit that for at least similar reasons as to why independent claim 2 from which all of the dependent claims 3-8 depend are believed allowable as discussed *supra*, the dependent claims are also allowable. The applicants however, reserve the right to address any individual rejections of the dependent claims and present independent bases for allowance for the dependent claims should such be necessary or appropriate.

Thus, applicants respectfully submit that the invention as recited in the claims as presented herein is allowable over the art of record, and respectfully request that the respective rejections be withdrawn.

CONCLUSION

Based on the foregoing amendments and remarks, the applicants respectfully request reconsideration and withdrawal of the pending rejections and allowance of this application. The applicants respectfully submit that the instant application is in condition for allowance. Entry of the amendment and an action passing this case to issue is therefore

[1] "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)."

respectfully requested. In the event that a telephone conference would facilitate examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided. Favorable action by the Examiner is earnestly solicited.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **50-4827**, Order No. 1700000-000010.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-4827**, Order No. 1700000-000010.

Respectfully submitted,
Locke Lord Bissell & Liddell LLP

Dated: February 16, 2009 By: _____

Serge Ilin-Schneider, Ph.D.
Registration No. 61,584

Correspondence Address:
Locke Lord Bissell & Liddell LLP
3 World Financial Center
New York, NY 10281-2101
(212) 415-8700 Telephone
(212) 415-8701 Facsimile